# An Address

ON

# ANCIENT HUMORISM AND MODERN HUMORISM.

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## I.

WHEN, after an interval of three years, our family of physiologists finds itself once more gathered together in formal congress, as we are at the present moment, we have many things to say to each other, and as the intensity of physiological research is considerable, it will be necessary to mention the definite progress that has been made after three years of labour. At this, our first meeting, therefore, it would be fitting that the new facts discovered by physiologists should be set before you. When, therefore, our illustrious President did me the great honour—an honour for which I am profoundly grateful to him—of selecting me as the first speaker, I first thought of giving you a brief account of the work accomplished since 1907. But very quickly I realized that such an account, even if I were capable of giving it, which is very doubtful, would be more like an analytical review than an academic discourse, and would be more of the nature of a book than of a speech.

Therefore I thought it wiser, though equally rash, to furnish, instead of a technical and bibliographical analysis, a more synthetic study—a general sketch of the tendencies of contemporary physiology.

## II.

Just as the traveller in the course of his journey, after having accomplished a fairly long stage, stops for a moment to look backwards and forwards, measuring with his eyes the distance he has covered and that which remains for him to traverse, so we, too, may ask ourselves what point we have reached and from what point we started: It is our right, our duty even, to seek in what direction is proceeding the evolution of the science which is dear to us—physiology—that science so useful in contributing to the welfare of mankind, to which all of us here present consecrate our teaching and our researches.

Now, it seems to me, upon reflection, that the physiological concepts of to-day might very well be expressed by a very old word, now perhaps a trifle out-of-date, "*humorism.*" All of us at this present moment are, consciously or unconsciously, humoralists—that is to say, we look upon the chemical constitution of our humours as being the basis of all biological phenomena; and we understand that word "humour" in the most general sense, for we not only think of the circulating or secreted humours, such as the blood, the bile, the milk, the urine, and the gastric juice, but also of the liquids which enter into the composition of our tissues; in other words, of all the chemical substances in solution of which the living organism is composed. It is by the chemical evolution of the substances contained in the plasmatic liquids that life is constituted.

And in conceiving life under this form we are only following a very ancient tradition. From the earliest times the composition of the humours has been regarded as of fundamental importance. Humorism had preoccupied not only physiologists, but also, and especially, physicians. For physicians have always been a little more theorists than physiologists, though the theories of medicine are always the direct outcome of physiological opinion. At all times, and perhaps more than ever to-day, physicians seek both their theory and their practice in the teaching of physiology. It matters little whether they acknowledge this or not; they follow the impulse that experimentation gives to the biological sciences. We are the creators, the innovators, the revolutionaries, and they conform to our conceptions. So much better if these conceptions are right. So much the worse if they are wrong. Medical theories are always the reflection of contemporary physiological theories.

It is not surprising, therefore, that the word "humorism" applies as much to medical as to physiological ideas. The physicians of the past were humoralists because the physiologists were so also. And as the physiology of the present day is essentially humoralist, modern medicine is necessarily so too, even at the risk of exaggeration. Medicine and physiology are merged in one another. Hippocrates, Galen, Van Helmont, the masters of humorism, did not think it necessary to separate the theories of life from the theories of disease.

And we must follow their example energetically, resolutely. There are not two biologies, that of the sick man and that of the healthy man. The laws are the same. We have a right to claim all the admirable work of contemporary experimental pathology as a part of physiology. I know very well that experimental pathology and physiology are taught from different chairs. But we admit that that fact is not of the least importance. The method is the same; the object is the same. The method, everywhere and always, is the experimental method; the object is, everywhere and always, the knowledge of biological phenomena.

## III.

The humorism of the ancients is very singular. According to Hippocrates, and—but for some slight shades of difference—according to Galen, life depends upon the humours. When they are in the right condition we have health; when they are corrupted we have illness. Nothing, you see, can be simpler.

What are these humours? Strange to say, Hippocrates, Galen, and all the physicians who followed them during sixteen centuries, describe humours which they had never seen, and which no one will ever see, for they do not exist. There was the blood, the yellow bile, the black bile, and the phlegm. The blood and bile have certainly an actual existence; but where is the black bile, which causes melancholy? And this extraordinary phlegm or pituitary secretion—this strange liquid, which is the cause of tumours, of chlorosis, of rheumatism, and cacochymia—where is it? Who will ever see it? Who has ever seen it? What can we say of this fanciful classification of humours into four groups, of which two are absolutely imaginary?

It was not until the advent of the great anatomists of the sixteenth century that the science of life emerged from the clouds in which it was enwrapped; it was not until the time of Harvey and Descartes that experiment triumphed over book learning. But what is truly extraordinary, what surpasses our wildest dreams, is the fact that for sixteen hundred years all physicians and all physiologists remained bound in the shackles of this incomprehensible error of the four cardinal humours. By what miracle was the spirit of conservatism or of routine able to hide the truth to such a degree? The men of science and the doctors of former times were no less intelligent than those of to-day. Nevertheless they accepted without a shadow of proof these childish theories; they could not see most simple facts, and they saw most complicated things which not only did not exist but which were not even probable. Is there not reason to be a little uneasy as to the fate reserved for our own work? Have we any assurance that our own conceptions will not be treated with contempt by our successors four hundred years hence? It is, therefore, prudent not to be too hard upon the past, because thus we may predispose those who come after us to show us a little indulgence.

With the Italian anatomists of the Renaissance, the orientation of physiology changed, in spite of the impotent efforts of Van Helmont; humorism was replaced by mechanism. It was thought that anatomy should be the guide of its servant, physiology. The dissection and opening of corpses became the basis of medicine and physiology. With the coming of Willis, Winslow, Morgagni, humorism was almost abandoned. And, after all, this was but just. How could it have any appearance of truth, since chemistry was not yet born?

It came into being, as you know, with Lavoisier, and with chemistry came medicine and physiology. The more I study the history of physiology the more do I look upon Lavoisier as the great initiator. It is useless to describe here his immense work. I will content myself with indicating it in a sentence that sums it up. Lavoisier understood, discovered, and demonstrated that life is a chemical phenomenon. At once all was clear. One understands the cause of animal heat, the *raison d'être* of respiration and alimentation; one grasps the meaning of energy; one applies the great principle of the transformation of the forces to general biology; and one can plainly foresee that humorism will triumph, and that the chemical transformations of which the organisms are the seat will be merged in the vital principle, which itself will have become superfluous. In spite of Galen, Descartes, Harvey, Haller, physiology begins with Lavoisier.

IV.

Nevertheless, the great scientific revolution which gave birth to chemistry did not immediately bear fruit. There were periods of uncertainty and hesitation, during which physiology and medicine, its faithful companion throughout the glorious nineteenth century, so fertile in discoveries, have oscillated, not knowing exactly from what side light was to come. And, in fact, just as the anatomists of the Renaissance guided biology from the side of dissection, so the micrographers, with their more and more perfected microscopes, have appeared to draw physiology towards histology, histogenesis and cellular morphology. Now, even if magnificent discoveries have been made as to the structure of cells; if it has been found possible to describe their forms, and the transformations of their granules; if, finally, it has become possible to consider the cell, which appears so simple an element, as an extremely complicated world in itself, nevertheless it seems to me that all this progress in morphology has done nothing towards elucidating questions of physiology. The greatest physiologists, on various occasions, have laid stress on the inadequacy of anatomy—even the most delicate microscopic anatomy—to elucidate the modality of the functions. This was one of the ideas dear to Magendie, and especially to Claude Bernard, who never tired of repeating that histology can do nothing, or next to nothing, for physiology, and that the knowledge of a form in nowise implies the knowledge of a function. It seems to me that one cannot possibly exaggerate in this direction. Even if we are able to describe minutely the form of a cell and the complicated network of the different granules which constitute it, we shall not have got much further towards knowing its proper function. Granted that a nerve cell contains two or three groups of matter which will take a different stain, how does the knowledge of that fact help us to know the quantity of oxygen it consumes, to determinethe conditions of reflex action and the laws of its irritability? Let us suppose that we have fathomed the structure of the muscular fibre, what will it teach us of muscular contraction?

Happily physiologists have not allowed themselves to be misled by the mirage of the microscope; they have studied physiology as physiologists, not as histologists; by chemical and physical experimentation, not by morphology. It is evident that neither Claude Bernard, Helmholtz, nor Ludwig refused to admit the use of it; but they always declared that its use was limited. They always preferred experiment to observation. They always preferred to analyse a function rather than to describe a form. It is for this reason that they made such noble discoveries, for the histology of an organ does not by itself lead to the discovery of the function of that organ.

V.

But medicine has not been as wise as physiology. It believed that microscopic anatomy, normal or pathological, was going to clear up everything, and we are forced to admit that it has hardly derived any profit at all therefrom. The whole history of cellular pathology, despite the genius of Virchow, has ended in a rather lamentable failure. Two or three of Pasteur's experiments have done more towards the renovation of medicine than fifty years of pathological anatomy.

And if I speak of Pasteur, of his glorious successors, R. Koch and Ehrlich, as I might speak of the eminent bacteriologists of the present day, it is because experimental pathology becomes mingled with pathological physiology, though not with morbid anatomy. It is not the microscopic observation of forms that has given us these marvellous discoveries by means of which the medicine of the past has been completely overthrown. Every branch of medicine has been regenerated—etiology, pathogeny, hygiene, therapeutics. It has been a revolution without precedent in the history of science. And this progress is due solely to experimentation—that is to say, to the methods of the physiologists. The morphology of bacteria is of little importance compared with the biology of bacteria.

Nevertheless, at the beginning of bacteriology, it seemed as though there was to be a definitive movement away from humorism. But important discoveries very quickly showed that, even for the study of microbes, it was necessary for the application of phenomena to come back to biologico-chemical analysis—that is to say, to humorism—for the understanding of microbes.

First came the fine discovery of Roux, which proved that the symptoms produced by the living and developing microbes are more or less identical with the symptoms caused by chemical substances which contain microbes. By injecting the soluble products contained in the microbes of diphtheria, the symptoms of that disease, which is due to the multiplication of diphtherial microbes, are reproduced. Some time afterwards I showed, in conjunction with Héricourt, that there are in the blood chemical substances capable of producing immunity. This was the principle of serumtherapy, which was so brilliantly applied by Behring two years later to diphtheria. And on all sides, with admirable enthusiasm, both doctors and physiologists, without stopping to ask if their work belonged to the domain of medicine or to that of physiology, studied the chemical functions of the blood, and have discovered in it manifold properties, the complexity of which increases every day. This is humorism in the strictest sense of the word.

You see, therefore, that although physiology has from the beginning been attached to humorism, medicine oscillated for a long time between contrary tendencies, leaning turn by turn towards anatomy, histology and bacterial morphology, but finally reverting to humorism, following the way pointed by the physiologists.

VI.

It is hardly necessary to point out that this modern humorism differs profoundly from the humorism of the ancients. In order to make you better understand the abyss which divides contemporary science from the conceptions of the past, I should like to show you in a very simple form—which I will try to present under the form of laws—the principal data of the humorism of to-day. To tell the truth, I reproach myself a little for using so pretentious a word as "laws." They are not laws, but rather generalizations of facts. It is no longer, as in the days of Hippocrates and Galen, a question of more or less undemonstrable theories, but rather positive facts, demonstrated and incontestable.

The first law is the following; it is founded on an incalculable number of facts:

*The quantities of substances which come into play in physiological reactions are often in such minute proportions that they may be called imponderable.*

This, first of all, calls for a definition of that which is ponderable. The limit of it is shown by the delicacy of our balances. One can weigh with a certain degree of exactitude a tenth part of a milligram, though that itself is a sufficiently delicate measure; but further we cannot go, and when we have to do with a hundredth part of a milligram, we have no means of determining such a weight. All the same, we are able to speak of a hundredth part, a thousandth part, a millionth part of a milligram; because, by dissolving a milligram in a litre, we get a thousandth part of a milligram in a cubic centimetre; by dissolving it in a cubic metre, we get the millionth part of a milligram in a cubic centimetre. But no chemical reagent, however sensitive, can reveal the presence of this infinitely minute amount. Nevertheless, certain physiological reactions allow us to demonstrate the action of these prodigiously diluted substances. I will give you some examples.

VII.

In seeking to discover the action of metallic salts on the acid fermentation of milk—a transformation of lactose into lactic acid—I have been able, by the use of very delicate acidimetric processes, to measure very minute differences between the quantities of acid contained in the fermented liquids. For example, I have been able to determine that in certain milks the quantity of acid was 100, and in others 100.5. This slight difference would signify nothing if one were content with analysing two flasks: the Flask A has 100, the Flask B 100.5. Manifold influences, impossible to determine with exactitude, may easily have slightly accelerated the process of fermentation in the flask of which the acidity is 100.5. But if, instead of using only two flasks, I use 2,000—1,000 flasks of Milk A and 1,000 flasks of Milk B—and if I find almost invariably that there is a difference of 0.5 per cent. between Milk A and Milk B, I am warranted in concluding with absolute certainty that there is in the flasks containing the Milk B an influence which is not negligible, and which accelerates the fermentation.

It is in this way that I have been able to establish that sometimes quantities of metallic salts corresponding to the frightfully small dose of the ten-millionth of a milligram per litre (in the case of the vanadium salts, for instance), were not without some effect on the lactic fermentation. This figure is altogether extraordinary, for the ten-millionth of a milligram exceeds in infinity all that we are accustomed to take into consideration.

Nevertheless the lactic ferment is discernible, distinctly discernible, in this amazing dilution, and as there is in a litre which is fermenting a hundred thousand milliards of cells, and perhaps more, it follows that the quantity of vanadium which acts on each cell is indicated by a fraction of a gram so small that twenty-five zeros would be needed to express it. All metals act almost in the same way as vanadium, notably thallium and barium. One may, therefore, ask oneself if it is a case of chemical action or of an action more or less analogous to that of radium. My lamented friend P. Curie formerly gave me a little radium emanation, that is to say, a gas in such small proportion that it is imponderable (one is not even yet certain that this emanation is a gas); in any case it has been possible to mix this emanation, already greatly diluted when Curie gave it to me, with 1,000 times its volume of air without its ceasing to exert an action on the lactic ferment. There is, therefore, ground for asking oneself if this action of the diluted metallic salts, that of the emanation of radium, to which the action of mineral waters is now compared, is chemical or physical? Is there not a transformation of energy? When the chemical action is transformed into other energies it becomes in certain cases perceptible to our senses even when it is very slight. Thus the light of a bright acetylene flame during one second represents only 1 cg. of carbon; nevertheless, it is perceived at the distance of 1 kilometre, that is to say, over an area of a square centimetre, making part of a sphere the radius of which is 1 kilometre. The very minute quantity of luminous energy set free by the thousand-millionth part of a milligram of carbon is still perceived by our retina.

In truth nothing permits us to suppose that these phenomena are not chemical; for we do not know the limit of the sensitiveness of living cells to chemical action. All that we can say is that the cells are extremely sensitive to chemical excitations. I can give you some examples of this.

It cannot be supposed that the olfactory sensibility is due to an excitation which is not chemical in nature. An odour is perceived when some particles of material substance come in contact with the olfactory mucous membrane, and this contact is necessary. But what infinite smallness! How calculate the quantity of matter that a hare leaves behind it in crossing a field? Nevertheless, it is enough to enable a dog to find the scent two hours later. Berthelot proved that in making a sufficiently rapid current of air pass over iodoform the smell of the iodoform is very distinctly perceived in the air that has passed. Nevertheless, the weight of the iodoform remains almost the same, although its smell is perceived in each one of the millions of litres that have been in contact with it. Berthelot was accustomed to cite another fact of the same order, but of rather uncertain interpretation. When one rubs copper lightly a certain characteristic odour is liberated, and yet the copper does not lose in weight.

M. Engelmann made a very curious experiment. Certain infusoria contain in their cell some granules of chlorophyll. Now if these infusoria are made to live in a liquid containing bacteria, and they are exposed for only a second to a ray of the sun, at once all the bacteria are seen precipitating themselves towards the chlorophyllian infusorium. This is because the infinitesimal quantity of chlorophyll exposed to light during a second has decomposed a particle of the dissolved carbonic acid and liberated oxygen which attracts bacteria. And, of course, in such a case we have to do with an imponderable quantity. But this quantity has been sufficient to make the bacteria precipitate themselves with violence towards this thousand-millionth part of a gram and a still smaller quantity of oxygen that has been given off.

The quantities of iodine found in the blood are in such small quantity that they cannot be measured. Often even one cannot detect any trace, and nevertheless, this iodine, which is found in imponderable proportions in the blood, may be—perhaps by the thyroid body—separated, isolated, accumulated, so that there is an iodine combination in the gland.

And as regards adrenalin secreted by the suprarenal glands and certainly poured into the blood, in what infinitesimal doses is it found in the blood of the suprarenal veins!

All chemiotaxis reveals to us the action of infinitesimal quantities. And in this chemiotaxis the history of the spermatozoa is of quite special interest. If they are attracted towards the ovum, that is assuredly by a chemiotactic force, and direct experiment proves that they are extremely sensitive to the weakest chemical action. If they are placed in contact with a drop of acid diluted to one-thousandth they are at once attracted. Now they move only because there is a difference of acidity between the quantity of acid found in the head and that in the tail of the spermatozoon; and this difference, if one thinks of the smallness of the cellular organism, exceeds in minuteness all that we can imagine.

In passing, it may be mentioned that embryology, which had hitherto remained a science almost entirely morphological, in which it might seem that humorism played no part, has now also entered on its humoral period. And forthwith great results have been obtained. The admirable researches of Delage have established the fact of chemical parthenogenesis, and the chemical—or osmotic, which is almost the same thing—influence of certain metallic salts even greatly diluted on the maturation of the ovum. So that chemistry—that is to say, humorism—dominates the penetration of the spermatozoon into the ovum, due to chemiotactic affinities as well as the maturation of the ovum and its embryogenic development. The chemical laws which govern the life of the adult also govern his birth. Certainly one is astonished when one sees a single cell by its proliferation become the origin of the immense aggregation of diverse cells which makes up the adult. But astonishment is still greater if one reflects that this development is the result of a chemical conflict, a conflict of substances altogether specific—since fecundation does not occur between different species—substances the absolute quantity of which is so small that it exceeds the limits of our understanding.

Experimentation with toxins furnishes us with examples just as remarkable.

Allow me in connexion with this to speak to you of a fact which I discovered some years ago, and which I called *anaphylaxis*. Thanks to the ardour and talent with which on all sides this new law of general physiology has been studied, it has assumed a great importance in physiology, and especially in pathology.

Anaphylaxis is the opposite of protection (phylaxis). If one injects an albuminoid substance—for example, a toxin—into the circulatory system of an animal, instead of being protected by this first injection against a further injection of the same toxin, it has become more sensitive to its action. Let us suppose that the fatal dose is 1 cg. The injection of a tenth part of that dose—that is to say, 1 mg.—will not make it at all ill, or scarcely so. But a month later—for almost a month is required for the anaphylactic state to be produced—it has become so sensitive that a dose of 1 mg. is enough to kill it by the immediate production of formidable symptoms. Therefore the first injection has caused a condition which is the opposite of protection—namely, anaphylaxis.

The sensibility of certain animals, notably guinea-pigs, to this first injection, which produces the anaphylactic condition, is altogether extraordinary. Two American physiologists, Rosenau and Anderson, have made a curious experiment on this point. They inject guinea-pigs with a very inoffensive serum, namely, horse serum; and they have satisfied themselves that horse serum has sometimes an anaphylactic effect in the inconceivably small dose of one-hundred-thousandth part of a cubic centimetre. In other words, a guinea-pig which a month before received the hundred-thousandth part of a cubic centimetre of horse serum, is never again altogether the same as a normal guinea-pig. If at the end of a month it receives another injection of a dose of horse serum, perfectly harmless to a normal guinea-pig, this will kill it in a few minutes. Now, the chemical albuminoid substance in horse serum which produces anaphylaxis is probably in very small proportion; it perhaps contains only one-thousandth part of the active substance, perhaps even less; in any case we learn from this curious experiment that a thousand-millionth part of a gram is still an active—a very active—quantity.

Another American physiologist, Dr. Vaughan, has succeeded in extracting from ovalbumin a chemical substance, both albuminoid and crystallizable, which produces anaphylaxis when given in a dose of a thousand-millionth part of a gram.

Anaphylaxis is not the only way in which the influence of these infinitesimal quantities of substance is manifested. The history of haemolysis, which the splendid work of Hamburger, Bordet, and many others has made so precise, shows very clearly that the most minute proportions of certain definite chemical matters possess a powerful activity.

The injection of a toxin produces an antitoxin (the active substance of anaphylaxis), and these antibodies and toxogenins are almost absolutely specific. But this is not the most curious feature of their history. To every antigen there is a corresponding special antibody. To the diversity of antigens correspond the diversity of antibodies secreted. The tyrosine of vegetable origin and the tyrosine of animal origin appear identical, and yet, as my friend C. Gessard has shown, vegetable antityrosinase is not the same thing as animal antityrosinase. Nothing can give us a clearer idea of this rigorous specificity than the application of anaphylaxis to medico-legal research.

M. Uhlenhuth has made some very conclusive experiments on this subject. Nine guinea-pigs receive injections of some drops of blood, of unknown origin (man, dog, rabbit, ox, horse, sheep, tortoise, fowl, or guinea-pig). A month later each of these guinea-pigs receives an injection of serum (man, dog, or rabbit, etc.). Let us suppose that one animal dies, the one injected with the blood of a horse. From this we may conclude with absolute certainty that the blood of unknown origin which was injected into the guinea-pigs a month earlier was that of a horse.

In connexion with this subject a somewhat amusing experiment has been made. A watery extract of various tissues from an Egyptian mummy over 3,000 years old was made and injected into guinea-pigs, and a month later it was found that these animals had been made anaphylactic by means of human albumins; which justifies us in drawing the conclusion—otherwise very probable—that the chemical constitution of the human being 3,000 years ago closely resembled the chemical constitution of man to-day.

I could cite many other facts, but I think I have said enough to convince you that very small quantities of substance possess a considerable biological activity. I prefer to try to indicate to you what deductions are to be made from such cases.

To begin with, our method of study is different from the old methods.

Up to the present, if one wished to study a substance one determined it chemically, one endeavoured to isolate it, to prepare it in a state of relative purity. But nowadays a new biological chemistry has sprung into being, that of imponderables. The *Chemistry of Imponderables!* These are two words which seem terribly contradictory. For chemistry depends above everything on the balance, and here we are constrained to study bodies beyond the reach of the balance.

The chemistry of the imponderables becomes necessarily, therefore, the chemistry of functions, in quite a different sense from the chemistry of functions in organic chemistry. It is the chemistry of the biological functions of the humours.

Assuredly there is a certain amount of danger in studying bodies that one cannot isolate, in giving them names, in describing their properties without having seen them, without having isolated them in the slightest degree, knowing, on the contrary, that they are mixed together with a great number of similar bodies. This is a real danger which must be taken into account—all the more because we have seen Hippocrates, Galen, and the old masters of medicine describe humours which existed only in their imaginations! Nevertheless, here we are dealing not with hypotheses, but with positive experiments. Here, let us say, we have a cubic centimetre of serum containing, besides the normal substances of serum, an anticoagulating substance, an anaphylactizing substance, or toxogenin, a lipase, a glycase, an antihaemolytic substance, a diphtherial antitoxin, a tetanus antitoxin, and if the unfortunate animal from which the serum is to be taken is capable of resisting other injections of antigens, its serum may contain many other antibodies besides. It would be an utter impossibility to isolate these different substances, the properties of which are very similar, though certainly not identical. Let us content ourselves by studying the chemico-biological functions of this drop of blood, which is a world in itself, and which possesses very strongly-marked properties — properties that a sagacious and scientific experimentation is going to reveal to us.

We are as yet only at the beginning of this chemistry of imponderables founded upon the analysis of biological functions, and nevertheless we can already foresee several of its consequences. It leads us directly into a region which up to the present day was almost totally unexplored—that is to say, into the physiology of the individual.

Till to-day investigators have concerned themselves almost entirely with the physiology of the species. One endeavoured to learn the conditions of existence of rabbits, dogs, cats, and guinea-pigs, and it was believed that the different individuals of the same species were identically the same, which is, in truth, very nearly the case. What is true of one rabbit would be applicable to another rabbit of the same size, sex, nourishment, and colour. But, as a matter of fact, such identity does not exist. In the vast forest there are no two families identically alike. No two animals are ever identical. It is certain that there are between them both anatomical and functional differences. Therefore it would be most interesting to physiologists to go further than they have yet done to determine these different characters; in a word, to work at the physiology of the individual after having studied the physiology of the species. To determine in what degree the individuals of the same species differ from each other would decidedly be a most useful and fertile discovery for physiology as well as for medicine.

Individuals of the same species differ in their psychological characteristics. This fact does not surprise us, since it has been a matter of common knowledge for a long time. The differences are all the greater the higher we go in the scale of mental development. In the human race the psychological differentiations which give to each individual a special character are most strongly marked. Each of us has a personality which differs very sharply from every other human personality. Memory, which has fixed in each of us the recollection of dissimilar events, accentuates all the more this intellectual variety which exists in us from the hour of birth. We are not surprised at it, for from the first beginnings of thought we have understood that our own "ego" differed from the "ego" of others in character, will, tastes, feelings, and memories.

We have, therefore, every one of us, a psychological individuality. But what has not been sufficiently taken into account is that each of us has also a humoral individuality. Each of us is differentiated from the rest of mankind not only by our mentality but by our chemical constitution. Since our humours contain an enormous number of imponderable substances, similar and allied, which most certainly exist in different proportions in different individuals, it follows that the humoral differences can be no less than the psychological differences. The more one analyses the chemical functions of the blood in different individuals, men or animals, the more one finds individual differences; and if, up to the present, homologous liquids belonging to animals of the same species have been identified, this is because it has only been possible to make an insufficient analysis.

Our chemical processes are too imperfect and too rough to reveal these differences to us. All the same we are able to affirm that they exist. The blood and humours of a person vaccinated ten years ago differ from the blood and humours of a non-vaccinated person. But will it ever be possible to isolate and determine this substance to which the vaccination has given birth in our organism?

Every illness, every intoxication, has caused the formation, perhaps the destruction, of a certain substance in the blood, and has left its natural trace, a trace which is not effaced by years. Just as there is the psychological memory, facts which are present to the consciousness, so there is a humoral memory of all preceding injections. As these injections differ in each person in intensity, quantity, and duration, it follows that each person differs from every other in the chemical properties of his blood.

It is useless to object that these differences are due, not to substances dissolved in the blood, but to leucocytes, and that it is by the modality of phagocytosis that individuals differ. According to the latest analysis, phagocytosis is a chemical phenomenon. The leucocytes have no activity save through the ferments they secrete, so that the differences of the phagocytes can be nothing else but a difference in chemical composition.

One might have hoped to discover a means of recognizing the individual humoral differences through the study of anaphylaxis. I have endeavoured to do so, but without success. This is how I proceeded. At first I tried to see how far it would be possible to transfuse the blood of one animal into another of the same species, and I found that one could inject into a dog 10 per cent. of his weight of pure dog's blood. A month later I injected the same dog with another 10 per cent. of blood taken from the animal from which the blood had before been transfused.

If there had been an individual anaphylaxis, there would have been at the second injection symptoms to which the first injection had not given rise; as if, for example, instead of two injections of dog's blood, I had given two of horse's blood. But the result of these experiments has been on the whole negative.

This by no means invalidates the fact of a strongly-marked humoral individuality, for anaphylaxis, notwithstanding all its precision, is still, like the rest, a somewhat rough process.

To sum up, as far as the law which is called the first law of humoralism is concerned, we can state positively that there exist in our humours innumerable substances, in infinitesimal and imponderable quantities, which, in spite of their minute proportion, play a considerable part in biological phenomena; and that, being in different proportions in each person, give to the humours of every individual a personal character, which differentiates him from all the other individuals of his own species.

We are, therefore, thoroughgoing humoralists; so much so that we can hardly suppose that the action of these infinitesimal quantities is exercised by the phenomena of ionization or osmosis. Whatever may be the importance of osmosis, it does not make itself felt when we have to do with the millionth part of a gram. It is certain that the mode in which these substances react is chemical, though we know little about the way in which chemical reactions operate in fairly strong dilutions.

Nevertheless we can foresee the modalities according to which these reactions of imponderable substances are effected. Certain remarkable and established facts relative to the function of certain glands, notably the pancreas, permit us to do so. The pancreatic trypsin has no digestive power; and as a matter of fact is it conceivable that there exists in a cell a substance which digests the cell itself? The pancreatic juice, isolated and gathered with minute precautions to guard against admixture with other liquids, is therefore deprived of all digestive activity, and the pancreatic cells contain no ferment. But they contain a "proferment," a pro trypsin, which can become extremely active under the influence of diverse chemical actions, and notably that of intestinal enterokinase. The active chemical substance A is therefore preceded by an inactive substance A′, which is its generator; and A′ becomes A when it is in presence of another substance B′ equally inactive. There will then be the following reaction, which is really very simple: $A' + B' = A + B$. It is probable that the quantities B′ necessary to bring about the reaction are very small, and it is possible that B′ does not disappear in this reaction. It is of little consequence; none the less, the matter stands as follows:

*The activity of a liquid results from the conflict of two substances which, isolated, are inactive.*

This is the second law of humorism, to which I call your attention most particularly, for it is of very wide scope. The haemolytic phenomena are due to the action of two substances, the properties of which it has been possible to study separately. The phenomena of anaphylaxis are likewise due to the combined action of two substances which are powerless when apart—namely, the antigen, which is in itself in a small dose ineffective, and the toxogenin which exists in the blood of an anaphylactized animal, toxogenin the slow formation of which has been caused by the injection of antigen; toxogenin which is in itself absolutely ineffectual and non-toxic, since anaphylactized animals live for a long time in perfect health; toxogenin which becomes a terribly deadly poison in the course of a few seconds when it meets with antigen, which likewise, in itself, is inoffensive.

Moreover, we find a striking example of these combined actions in an experiment well known to all physiologists since Claude Bernard. Amygdalin, from bitter almonds, is an innocent enough substance, as is also the emulsion, which is not at all poisonous. Now, if an animal is injected with a very small quantity of emulsion, having previously received an injection of amygdalin, immediate and appalling symptoms appear, for the result of the chemical conflict of amygdalin and emulsion, both harmless, is a terrible poison (hydrocyanic acid). Every time that a careful experiment has been made on ferments and toxalbumins, so nearly allied to the ferments, it has been ascertained that in the organisms ferments and toxins exist in the state of *proferments* and *protoxins*. The cell can only secrete a substance inoffensive for the cell; it would be absurd to suppose that it will produce that which is capable of killing or dissolving it. Therefore it secretes only a harmless substance, endowed with scarcely any toxic or fermentative properties. But this innocent substance, which is neither haemolytic, nor glycolytic, nor lipolytic, nor neurolytic, may become so when it encounters in its path another equally harmless substance. And the result of the reaction will be, according to the nature of the two bodies which come into play, or even of one of these bodies, the production of a substance either haemolytic, glycolytic, lipolytic, or neurolytic.

If most often we act upon ferments and toxins already formed, it is because we have not known how to prepare the protoxins and proferments. As a matter of fact, these preparatory bodies are probably of extreme instability, and transform themselves into real toxins and real ferments under very slight chemical influences, weaker than our laboratory reagents, which are violent and brutal, and whose action is not controlled. Thus, in order to arrive at a knowledge of these proferments we are nearly always obliged to study the organic liquids intact without having subjected them to any manipulations. The preparation and isolation of these bodies causes them to disappear, and the more one tries to purify them so much the faster do they disappear, as of old gold disappeared in the crucible of the alchemists.

We were speaking just now of the chemistry of the imponderables; now we have come to the chemistry of unstables. And certainly the difficulties are immense, but it is the interest of science that every step in advance leads us into a region the exploration of which is more laborious and more uncertain. Let us give this instability of chemical substances, humoral or biovular, its real name, its true physiological name—it is irritability. To be unstable is to be apt to modify one's self under the influence of the feeblest external actions; it is to be irritable by exterior actions, whether mechanical, physical, or chemical; all irritability—that is to say, the greater part of physiology—has for its basis the chemical instability of bodies which constitute the living being.

Thus, on the one hand, a substance is active, though the proportion of it is small; on the other hand, for the function of this substance, by the conflict of two substances which have been prepared long before, a very slight excitement, chemical or other, suffices. These two laws lead necessarily to a third, namely, that phenomena of great intensity may be produced suddenly, when a chemical cause, even a very slight one, intervenes. This chemical cause, which though infinitely minute leads to sudden and powerful effects, is produced by the nervous system. It is probably in this way that is to be explained that wonderful phenomenon which has justly attracted the attention of all physiologists—the action of the nervous system on the secretions. One of the masters of physiology, the great Pflüger, whose recent death we now deplore, a long time ago sought to discover nerve endings penetrating into secreting cells. This is not necessary in order to understand the phenomena of glandular excitement. We need not suppose that the nervous protoplasm comes into direct contact with the glandular protoplasm. It is sufficient to admit that a most minute fermentative reaction is produced from the beginning of the nervous tube to its ending, running along from point to point like a train of gunpowder, with a rapidity of 30 metres a second, and that at the extremity there appears a minute quantity of substance which is capable of acting chemically upon the secreting cells. The imponderability and the instability of the chemical substances of our organs are sufficient to explain this action. And perhaps it is by an analogous mechanism that the nerves act upon the muscles and determine reaction. Who knows even if the complicated actions of the soul, reflex or voluntary, the feelings and the emotions, are not also chemical phenomena, as Lavoisier has already remarked in words that have become famous. But I do not wish to allow myself to be carried away by hypotheses; it is enough for me to have established that the irritability of our tissues is the necessary and inevitable consequence of the two fundamental laws of humoralism—imponderability and instability. You see, therefore, that there is no need to place in opposition to each other the humoral and the nervous theories, inasmuch as the irritability which rules the functions of the nervous system is in itself a humoral phenomenon. And, by a wonderful concatenation, the nervous system acts at every moment on the chemical constitution of our humours, just as the chemical constitution of our humours reacts each instant on the nervous system. But in the case of the nerves, as in the case of the humours, it is chemistry that governs all. The living being is a chemical mechanism, and perhaps it is nothing more.

In any case its completion is astounding, and we might well be afraid, if we had not before us the example of our glorious predecessors. With resources very inferior to ours, with imperfect instruments, obsessed by ridiculous theories, they finished by bringing to light some truths from the ocean of darkness in which they were sunk. It is true that they were not always modest, and they often believed themselves to have grasped the truth when they had only got hold of illusion and error. There also let their example serve us as a lesson. Let us be bold in hypothesis. One is never sufficiently so. But let us also be very cautious in affirmation. For that which constitutes a true man of science is that he joins to extreme boldness in hypothesis extreme caution in conclusion. Especially, do not allow your patience to tire. Nature is rebellious, and does not allow the first comer all at once to tear from her her secrets. One only succeeds in learning these terrible secrets in fragments, and at the cost of long and laborious efforts. There is no need for me, gentlemen, to recall this to you who have disinterestedly given yourselves to the study of the great problems of life. It is not, therefore, to you that I speak, but I will speak all the same, for I should wish that my feeble voice could be heard louder and further.

Science to-day cannot progress without great pecuniary sacrifice. Science is costly. Instruments and laboratories, staffs and material—the expense increases every day with the increase of the difficulties of research. It is therefore necessary that public authorities and public opinion, which is superior to governments, should at last understand that physiology must be supplied with necessary arms. But, alas! it is other arms that are gathered on all sides. Never has the madness of militarism been so serious. All the energy that there is in peoples—energy in men and energy in money—is devoted to the fostering of absurd hatred and fratricidal rivalries. War—the war which ruins and desolates mankind—war takes all. And science—beneficent and fertile science—science has only the remains. Incredible and lamentable error, which at all times weighs on human destiny, and to-day more heavily than ever.

Do you wish for a striking example? Here it is. An admirable discovery has just been made. Man has just succeeded in constructing flying machines and in supporting himself in the air, in traversing space as rapidly and easily as a bird. We have some right here, gentlemen, to be proud, since it is the physiologists who opened the way for the brothers Wright. I can speak of it here before you, Mr. President, who have made such beautiful investigations on the flight of birds. And why should I not recall the memory of a great physiologist, my master Marey, who, with his profound sagacity, foresaw the triumph of the airman? And why should I not say—not, I admit, without some pride—that with my ingenious friend Zatin, in 1892, we constructed and floated the first aëroplane. Aviation, therefore, has its starting point in physiology, and it is well to record the fact here in a gathering of physiologists.

Well, poor man is brutalized by his warlike fury to such a point, that the conquest of the air by science and human industry has at once suggested to him the triumphant idea that the aëroplane is a marvellous engine of war. He has set before himself the glorious task of transforming an instrument of pacification into a murderous machine, and, excited by foolish journals, public opinion has become more violently warlike.

In the face of this immense human folly we, my dear colleagues, have a great duty. That is, to seek to dissipate ignorance, for it is by ignorance that men are made as bellicose as savages.

Let us combat ignorance and aid the coming of the kingdom of science, which knows no frontiers. Science makes existence happier and less cruel. It is entitled to the respect of all, for it prepares a less barbarous world for the men of the future.

Honour, therefore, to our science! Honour to physiology, which strives for the mitigation of the misery, the error, and the suffering of mankind!

# ABSENCE OF THE FALLOPIAN TUBES AND OF MENSTRUATION.

## MONTHLY RECURRING ATTACKS OF PERITONITIS: RELIEF FOLLOWING AN OPERATION JOINING OVARIAN POUCHES WITH THE UTERINE CAVITY.

By **W. G. SPENCER, M.S.,**
SURGEON TO THE WESTMINSTER HOSPITAL,

*With a Note*

By **ALBAN DORAN, F.R.C.S.,**
CONSULTING SURGEON TO THE SAMARITAN FREE HOSPITAL.

I AM much obliged to Mr. Alban Doran for his note on this case. He tells me that there is no similar case recorded in the *Transactions of the Obstetrical Society of London;* nor does there appear to be such a one included in the bibliography attached to Dr. J. W. Ballantyne's article in Allbutt and Eden's *System of Gynaecology*, second edition, 1906, p. 171; nor have I found any other reference.

*History.*

G. R., single, aged 28, a general servant, was sent into hospital in May, 1909, by Dr. Shillingford, of Peckham, complaining of attacks of pain in the right iliac region. The patient had never menstruated; she had never had a show of any kind. When aged about 18 she first felt sharp pains in the abdomen around the umbilicus, and such pains have recurred with fair regularity every month, usually lasting three or four days. Gradually the attacks of pain became more severe. They began by a strange feeling in the right iliac region; then, as the pain increased around the umbilicus, she felt faint, trembled, sweated, and had nausea. A very severe attack occurred in September, 1908, and another in the following November. Recently the umbilical pain had tended to spread